



Illicit drug use in Reykjavik by wastewater-based epidemiology

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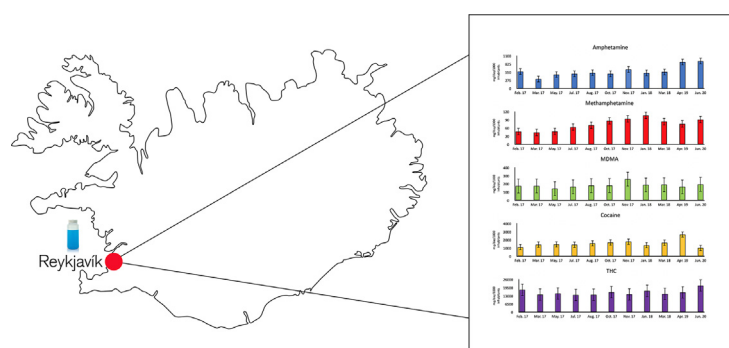
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HIGHLIGHTS

- First comparison of illicit drug use in Reykjavik by wastewater analysis with other indicators.
- Wastewater-based epidemiology was used to estimate cannabis use in Reykjavik for the first time.
- Results revealed increased use of cocaine and amphetamine from 2017 to 2019.
- Changes in patterns of drug use were observed during the COVID-19 pandemic.
- Comparison between three indicators of illicit drug use showed corresponding results.

GRAPHICAL ABSTRACT



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ABSTRACT

Estimation of illicit drug use on a community level by wastewater-based epidemiology (WBE) is both an objective and reliable way to establish near real-time results. Wastewater samples were collected at eleven timepoints in Reykjavik from 2017 to 2020. The use of commonly abused illicit drugs in Iceland (amphetamine, methamphetamine, 3,4-methylenedioxymethamphetamine (MDMA), cocaine, and cannabis) was estimated. Solid phase extraction and ultra-high performance liquid chromatography coupled to tandem mass spectrometry was used for analysis. Estimated amphetamine and methamphetamine use showed signs of an increase from 2017 to 2020 with amphetamine being the dominant stimulant on the market. MDMA use remained stable from 2017 to 2020. Results showed a large increase in cocaine use from 2017 to 2019 but interestingly, a marked decrease in 2020 during the COVID-19 pandemic. Cannabis use was stable from 2017 to 2019 but showed signs of an increase during the pandemic in 2020. Results by WBE corresponded with data based on two other indicators of drug use, seizure data and driving under the influence cases. Both temporal and spatial trends in illicit drug use were successfully estimated by using WBE, complimenting other indicators which provided a comprehensive picture of drug abuse in Reykjavik.

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1. Introduction

Availability and purity of illicit drugs is on the rise in Europe. This will result in harmful effects on human health and social welfare with increasing numbers of drug-related deaths (European Monitoring

Centre for Drugs and Drug Addiction, 2019; United Nations Office on Drugs and Crime, 2018). Wastewater-based epidemiology (WBE) has provided insight into the extent of illicit drug consumption since first applied in 2005 (Zuccato et al., 2005). Based on the analysis of illicit drugs in composite wastewater samples collected over 24 h, this methodology effectively monitors both temporal and spatial trends in drug use in an objective and rapid way (Castiglioni et al., 2014). WBE has shown clear advantages over other indicators of illicit drug use with

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known biases such as traditional survey methods (Castiglioni et al., 2014; Kankaanpää et al., 2016). Nevertheless, there are uncertainties associated with estimations based on WBE that are required to be addressed appropriately. The current available pharmacokinetic information on illicit drugs used in the determination of consumed amounts is limited as the data is often based on a small number of studies with few participants (Castiglioni et al., 2013). Excretion rates can also vary substantially between individuals, route of administration, and frequency of use. Therefore it is important to use excretion rates that represent the most common routes of administration for the target population, if available (Gracia-Lor et al., 2016). A recognized challenge of WBE is also the assessment of the population size behind a sample (Castiglioni et al., 2013). The documented census numbers can be insufficient as population contributing to the site is likely to vary e.g. due to tourism, commuting patterns, seasonal variability or special events (Lai et al., 2011). Several approaches have been used to estimate the population size (Baz Lomba et al., 2019; Lai et al., 2015; Lai et al., 2011). The appropriate approach for these estimations must be evaluated based on the available resources. Hence, it is important to take the known uncertainties of WBE into account when results are interpreted.

Since 2015, WBE has been used to investigate the stimulant drug market in Iceland. Results have shown high levels of amphetamine in wastewater compared to other European countries and recently a large increase in cocaine levels (González-Mariño et al., 2020; Löve et al., 2018). By only using WBE, it is however not possible to determine if these trends are due to changes in the number of drug users, number of consumed doses or changes in drug purity (Bruno et al., 2018). A more comprehensive picture of illicit drug use can be provided by complementing WBE with other indicators of drug use. These are e.g., driving under the influence (DUI) cases and data on seized amounts of drugs (Bruno et al., 2018; Kankaanpää et al., 2016).

Until now, information on illicit drug use in Iceland has mainly been obtained through self-reported consumer interviews and medical figures from rehabilitation centers (The Directorate of Health, 2012; Tyrfingsson, 2019). The National Centre of Addiction Medicine (SÁÁ) in Iceland aims to determine the most problematic substance for patients entering drug rehabilitation. As of 2015, cannabis was most frequently problematic for patients, followed by amphetamine and cocaine (Tyrfingsson, 2019). A survey on illicit drug use in Iceland conducted in 2018 (1277 individuals, aged 18 to 67) showed similar results with cannabis being most frequently used followed by amphetamine and cocaine (Kristjánsson and Jónsson, 2019). Organized crime groups in Iceland handle most import, production, sales and distribution of illicit drugs (National Police Commissioner of Iceland, 2019). An increase in cocaine import is considered an indication of a rising number of these crime groups in Iceland (National Police Commissioner of Iceland, 2019). Now with record breaking numbers of cocaine seizures in Europe, high availability of the drug has led to a considerable increase in purity (European Monitoring Centre for Drugs and Drug Addiction, 2020). This poses a risk to users that are accustomed to lower doses, leading to an increase in drug related deaths and rising numbers of users who seek help for cocaine dependence (National Police Commissioner of Iceland, 2019; Tyrfingsson, 2019). With higher availability and purity of drugs with rising numbers of users, it is important to closely observe new trends in illicit drug use so appropriate preventative actions can be taken.

For the first time, this study aims to compare illicit drug use by WBE with statistics on positive DUI cases and seized amounts of drugs by the police. Tetrahydrocannabinolic acid (THCA) is the main metabolite of tetrahydrocannabinol (THC), the active component of cannabis, in urine. Data based on the analysis of THCA in wastewater was used for the estimation of cannabis use in Reykjavik. Results on THCA in Icelandic wastewater have not been reported before. The objective is to provide a clearer picture on the extent of illicit drug use in Iceland and determine trends in use.

2. Materials and methods

2.1. Chemicals and materials

Amphetamine hydrochloride, benzoylecgonine (BE), cocaine hydrochloride, methamphetamine hydrochloride, 3,4-methylenedioxyamphetamine (MDMA) hydrochloride and d,l-11-Nor- Δ^9 -tetrahydrocannabinolic-carboxylic acid were purchased from Lipomed (Arlesheim, CH). Corresponding isotope-labeled internal standards (ILIS) amphetamine-d3 and cocaine-d3 were purchased from Lipomed (Arlesheim, CH). Benzoylecgonine-d3, MDMA-d5 and methamphetamine-d5 were purchased from Sigma-Aldrich (St. Louis, MO, USA). 11-nor-9-carboxy- Δ^9 -tetrahydrocannabinol-d3 was purchased from Cerilliant (Round Rock, TX, USA). Reference standards and internal standards were in methanol (MeOH), ethanol (EtOH) or acetonitrile (ACN) at concentrations of 1 mg/mL or 100 μ g/mL. MeOH and formic acid were purchased from Sigma-Aldrich (St. Louis, MO, USA) and ACN was from Honeywell (Charlotte, NC, USA). Water was purified using a Milli-Q Integral 3 water purification system. Oasis HLB 3 cc Vac solid phase extraction (SPE) cartridges (60 mg sorbent, 30 μ m particle size) were purchased from Waters (Milford, MA, USA).

2.2. Sample collection and storage

Sample collection was carried out from two WTPs, Skerjafjarðarveita and Sundaveita. Approximately 90.000 individuals contribute to each of these WTPs which is around 80% of the population in the Reykjavik metropolitan area combined. Details on the residential population at each time of sample collection is presented in Table S4 in the supplementary information. The two WTPs only perform coarse screening with sedimentation of large solids before the wastewater is released directly into the ocean. The residence time in these WTPs is short with no aeration, resulting in negligible biological degradation. Wastewater was collected after the coarse screening at eleven time points from 2017 to 2020. Normal weeks were selected for sample collection representing baseline consumption, except for one week where a music festival was held in Reykjavik. 24 h samples were collected in time-proportional mode over seven days in 2017 (February, March, May, July, August, October, and November), 2018 (January and March), 2019 (April), and 2020 (June). Sample collection in 2019 and 2020 was only conducted in Sundaveita WTP. Samples were kept frozen ($-20\text{ }^{\circ}\text{C}$) without adjustment of pH until analysis.

2.3. Sample extraction procedure

A SPE procedure for sample preparation was based on Bijlsma et al. (2014) and carried out as follows: Oasis HLB cartridges were conditioned with 6 mL of MeOH and 6 mL of purified water. 50 mL aliquots of wastewater samples were centrifuged after the addition of ILIS (180 ng/L). The supernatant of the wastewater sample was then loaded onto the cartridges. The cartridges were washed with 3 mL of purified water after loading and vacuum dried for 15 min. The analytes of interest were then eluted off the cartridges with 5 mL of MeOH. The eluate was evaporated at $40\text{ }^{\circ}\text{C}$ to dryness and the residue was reconstituted in 1 mL MeOH. 5 μ L were injected into the ultra-high performance liquid chromatography tandem mass spectrometry system (UHPLC-MS/MS) for the analysis of THCA. A 50 μ L aliquot of the final MeOH extract was further diluted in 450 μ L of purified water and 5 μ L were injected into the UHPLC-MS/MS for the analysis of amphetamine, methamphetamine, MDMA and benzoylecgonine.

2.4. Instrumental conditions

Instrumental analysis was performed using Waters Acquity UPLC I-Class system, consisting of a column manager, sample manager (fixed loop) and a binary solvent manager. A Waters Acquity UPLC® BEH

C18 column, 1.7 μm , 2.1 \times 100 mm (Milford, MA, USA) was used for chromatographic separation with a column temperature of 40 °C. A constant flow rate of 0.4 mL/min was held with a mobile phase consisting of 0.1% formic acid in water (solvent A) and ACN (solvent B). The gradient was as follows: 2% B from 0 to 1.5 min, 13% B at 1.8 min, 36% B at 2.65 min, 50% B at 3.4 min, 95% B at 3.45 min, 2% B at 2.8 min.

The UPLC system was coupled to a Xevo TQ-S micro mass spectrometer with a step wave ion guide and electrospray ionization (ESI). The cone gas was nitrogen with a gas flow rate of 20 L/h, the desolvation gas was nitrogen with a gas flow rate of 800 L/h and the collision gas was argon. Capillary voltage was set to 1 kV. The source temperature and desolvation temperature was 150 °C and 500 °C, respectively. Selected quantifier and qualifier transitions along with other MS/MS parameters for each compound are presented in Table S1 in the supplementary information.

2.5. Method validation

The methodology was validated before analysis according to guidelines published by the European Medicines Agency (EMA), the International Union of Pure and Applied Chemistry (IUPAC) and the Scientific Working Group for Forensic toxicology (SWGTOX) with appropriate modifications (European Medicines Agency, 2011; International Union of Pure and Applied Chemistry, 2002; Krueve et al., 2015a, 2015b; Scientific Working Group for Forensic Toxicology, 2013). The following validation parameters were tested: linearity, accuracy, precision, recovery, and matrix effects. A detailed description of validation experiments can be found in the supplementary information.

2.6. Calculations

Daily mass loads (mg/day) of each analyte in wastewater were calculated per 1000 inhabitants. The mass loads were obtained by multiplying the measured concentration (ng/L) of each analyte or their metabolite in wastewater by the average wastewater flow rate (L/day). The consumed amounts were obtained by multiplying the mass loads by a correction factor. The correction factors are based on excretion percentages in urine and molecular mass ratio between the parent compound and metabolite (if applicable). Correction factors used in the calculations are presented in Table 1 along with mean excretion rates and molecular mass ratios. The excretion rates are either based on the weighted mean for different routes of administrations or, if available, the most appropriate route of administration for the target population (Castiglioni et al., 2013; Gracia-Lor et al., 2016). The daily consumed amounts were finally divided by the population of each WTP, based on census data, and normalized by 1000 inhabitants (mg/day/1000 inhabitants). Population numbers were obtained from Statistics Iceland and are based on registered residences in different postal codes of the Reykjavik area for each year. Consumed amounts were back-calculated using correction factors as opposed to population normalized mass loads to allow for a reliable comparison with epidemiological data. Parameters used in the calculations of used amounts of illicit drugs are listed in Table S4 in the supplementary information.

Table 1

Correction factors for each analyte used in the back-calculations and parameters used to obtain them (mean excretion of drug target residue and molecular mass ratio).

Drug target residue	Mean excretion (%)	Route of administration	Molecular mass ratio	Correction factor
Amphetamine	36.1 ^a	Oral	1.00	2.77 ^a
Methamphetamine	39.3 ^a	Intranasal	1.00	2.54 ^a
MDMA	22.5 ^b	Oral	1.00	4.40 ^a
Benzoylcgonine	29.2 ^a	*	1.05	3.59 ^b
THCA	0.500 ^a	Smoked	0.910	182 ^a

* Weighted mean of excretion percentages for different routes of administrations.

^a (Gracia-Lor et al., 2016).

^b (Castiglioni et al., 2013).

2.7. Comparison with other indicators of drug use

In this paper, results by WBE are compared with data on DUI cases and seized amounts of drugs by the Icelandic police.

Data on both the number of positive and negative DUI samples from 2014 to 2020 were obtained from the Department of Pharmacology and Toxicology (DPT), University of Iceland, where all Icelandic DUI cases are handled. Data collection by the DPT is based on the type of analysis requested by the police. Requested analysis by the police is based on preliminary testing of amphetamines, cannabis, and cocaine. Amphetamines are analyzed as a package which included amphetamine, methamphetamine and MDMA.

Data on seized amounts of illicit drugs was provided by the National Commissioner of the Icelandic police. This data contained information on seized amounts of illicit drugs from the year 2014 to 2019. Seized amounts of amphetamine is presented in both grams (powder form) and milliliters (liquid form). Seized amounts of methamphetamine and cocaine is presented in grams (powder form). Seized amounts of MDMA in both grams and pieces (tablets) was provided. Seized amounts of MDMA tablets was transformed to grams by multiplying the average weight (mg) of tablets received for analysis at the DPT from 2010 to 2019 by seized amounts of tablets by the police, divided by the average concentration of MDMA crystals received for analysis at the DPT from 2012 to 2019. Data on seized amounts of cannabis included the number of plants in active soil cultivation, grams of cannabis plants in the drying process, grams of marijuana ready to be sold on the drug market and grams of hash.

3. Results and discussion

3.1. Method validation

The performance of the analytical method met requirements presented in the validation guidelines for all analytes (European Medicines Agency, 2011; International Union of Pure and Applied Chemistry, 2002; Scientific Working Group for Forensic Toxicology, 2013). Wastewater from Reykjavik consists largely of tap water due to high water usage of the population. Therefore, tap water was selected as a background matrix for validation experiments as drug free matrix was not available. Results for accuracy and precision (within-day precision and intermediate precision) were within acceptable criteria and are presented in Table S2 in the supplementary information. Recoveries ranged from 93.7% to 113%. Linear regression (R^2) was >0.99 for all analytes. Matrix effects in tap water were estimated to be within 15% for all analytes except THCA and was compensated for by using corresponding internal standards. The reliability of results was confirmed by participation in yearly inter-laboratory experiments where all selected analytes met criteria (van Nuijs et al., 2018). Results for matrix effects, recovery and linearity are presented in Table S3 in the supplementary information.

3.2. Amphetamine

The route of administration of illicit drugs in Iceland is not well described especially in the case of amphetamine. Heavy consumption is likely through intravenous injection, whereas more numerous recreational consumers depend more on nasal or oral effects (Tyrfingsson, 2019). However, very little data on excretion rates of amphetamine for different routes of administrations is available except for the oral route (Gracia-Lor et al., 2016). Therefore back-calculations of amphetamine use in Reykjavik by WBE are based on excretion rates after oral consumption.

Results from the analysis of amphetamine in wastewater samples collected in Reykjavik at eleven different time points from February 2017 to June 2020 are presented in Fig. 1. Results showed a significant increase ($p < 0.05$, t -test) in amphetamine use by 61% (from 571 to

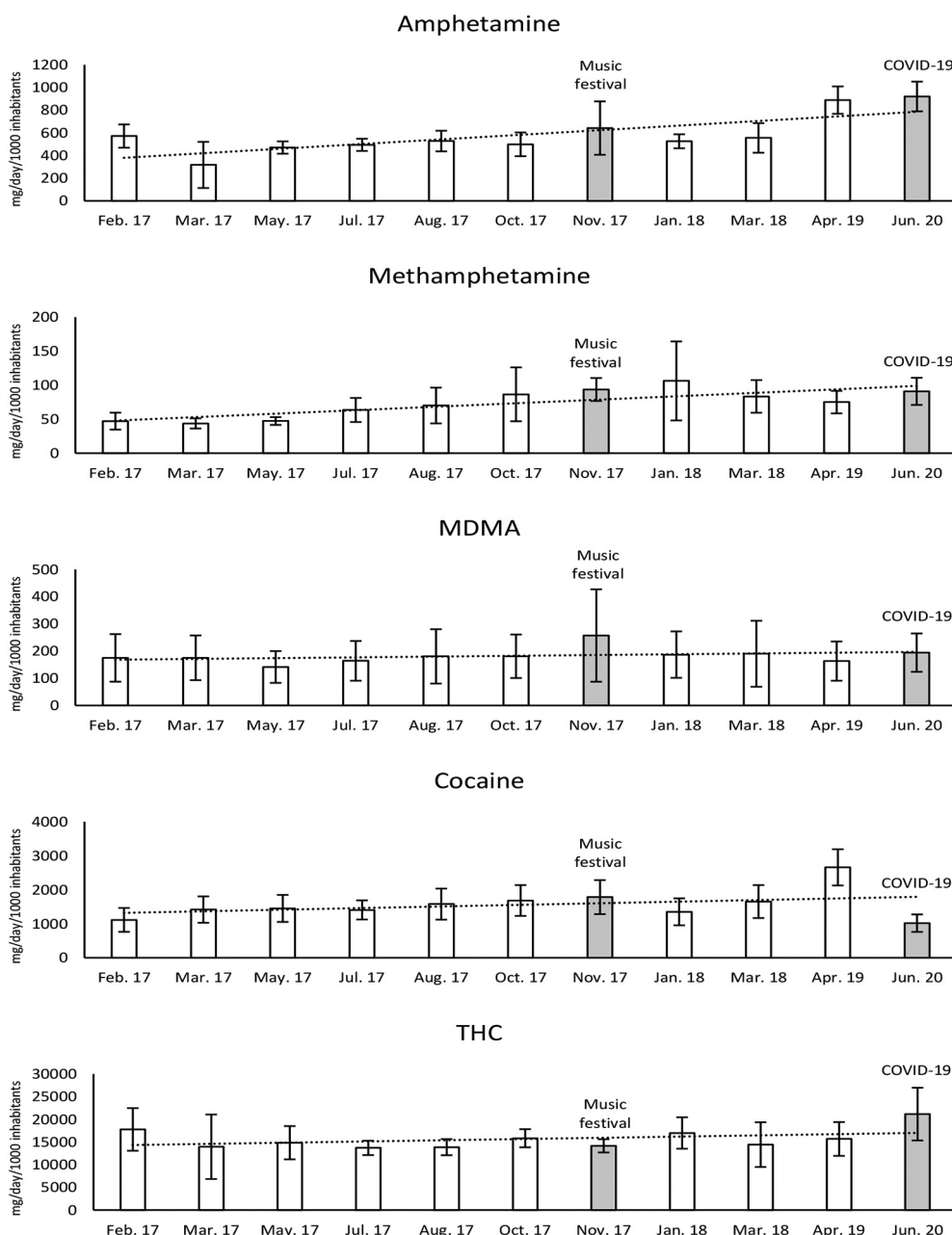


Fig. 1. Estimated use of amphetamine, methamphetamine, MDMA, cocaine and cannabis in Reykjavik in mg/day/1000 inhabitants during eleven weeklong sampling periods between February 2017 and June 2020.

920 mg/day/1000 inhabitants). Amphetamine use was relatively stable from February 2017 to March 2018 but had increased significantly ($p < 0.05$, t -test) by 60% in April 2019 (from 555 to 888 mg/day/1000 inhabitants). Results from the analysis of wastewater samples collected during the COVID-19 pandemic in June 2020 showed similar levels as in April 2019 (921 mg/day/1000 inhabitants). At the time, restrictions were on gatherings and opening hours of nightclubs, restaurants, and cafés. The population size in each area could be affected by decreased mobility during the pandemic, compared with previous sampling periods, which is not detected in changes in the residential population. Fluctuations in the population could be a source of uncertainty for back-calculated population normalized amounts which should be taken into consideration when interpreting results. More detailed information on the population size for example through mobile data could give a better understanding of these variations although it was not available for the present study. These results indicate that there were

minimal effects due to the pandemic on amphetamine use at that time. Nevertheless, it should also be noted that only one sample collection was conducted in both 2019 and 2020 and therefore seasonal variability could affect these results. Overall, the data presented shows signs of increased use of amphetamine in Reykjavik. Previous studies on spatial trends have reported high amphetamine loads in wastewater from northern European cities, including Reykjavik, Oslo, Stockholm, and Helsinki, compared to southern parts of the continent (González-Mariño et al., 2020; Löve et al., 2018). Results showed up to a 31% increase in amphetamine use during weekends (Saturday to Sunday). Although increased use of amphetamine during weekends was only considered significant ($p < 0.05$, t -test) in six out of eleven sampling periods, the results indicate that the drug is used recreationally to some extent. A music festival (Iceland Airwaves) was held in Reykjavik during the November 2017 sampling period (from Thursday to Sunday). The results showed a 66% increase in amphetamine use during the music

festival compared to other weekdays with a large spike on Friday (103% increase from Thursday) but had dropped again from Saturday to Sunday. These results indicate that amphetamine is used as a recreational drug during special events.

The number of positive DUI cases for commonly used illicit drugs from 2014 to 2020 is presented in Fig. 2. The number of positive DUI cases increased steadily by 117% from 2014 to 2019 (from 514 to 1120 cases) but decreased by 20% from 2019 to 2020 (from 1120 to 886 cases). The number of positive cases was relatively stable from 2014 to 2016 but increased by 81% from 2016 to 2019 with the largest leap between 2016 and 2017 (43% increase). However, the total number of performed tests increased by 40% from 2014 to 2020. These results nevertheless suggest that the total number of amphetamine consumers is growing, resulting in an increased number of positive DUI cases. This is in accordance with data by WBE which also indicates increased amphetamine use. A rising number of patients in rehabilitation centers since 2014 further supports this trend (Tyrfinngsson, 2019). The decrease in DUI cases in 2020 could be explained by the social disruption caused by the COVID-19 pandemic. Decreased mobility due to e.g., restricted opening hours of restaurants, cafés and nightclubs could have affected the number of DUI cases.

Data on seized amounts of amphetamine from 2014 to 2019 in both powder and liquid form is presented in Fig. 3. Yearly data from the Icelandic police on seized amounts of amphetamine in powder form shows considerable fluctuations during the six-year period presented (2014 to 2019) with a range from 4.9 kg to 56 kg per year. It was not possible to detect similar trends in seized amounts of amphetamine powder compared to the number of positive DUI cases and data by WBE. Seized amounts of amphetamine in liquid form, amphetamine base intended for local production of amphetamine powder, also shows significant fluctuations over the six-year period. The total amounts of seized amphetamine base from 2014 to 2016 was negligible but increased greatly from 2017 to 2019. The extensive increase in seized amounts of amphetamine base in the past 3 years suggests that the production of amphetamine powder is on the rise in Iceland. Overseen by foreign criminal organizations, the supply of amphetamine in Iceland is stable indicating an abundance of amphetamine on the market (National Police Commissioner of Iceland, 2019). An increase in local production of amphetamine would support data by WBE and the number of positive DUI cases with an increasing number of amphetamine users and/or the concentration of the drug.

3.3. Methamphetamine

Results from the analysis of methamphetamine in wastewater samples collected in Reykjavik from February 2017 to June 2020 are presented in Fig. 1. Methamphetamine use according to WBE increased

significantly ($p < 0.05$, t -test) by 94% during the total sampling period from February 2017 to June 2020 (from 47.1 to 90.9 mg/day/1000 inhabitants). A significant increase ($p < 0.05$, t -test) in methamphetamine use by 125% was observed from February 2017 to January 2018 (from 47.1 to 106 mg/day/1000 inhabitants), but amounts had dropped by 20% in March 2018. The results showed stable use from March 2018 to June 2020 indicating minimal effects caused by the COVID-19 pandemic. These trends could point to a shifting methamphetamine market in Iceland where the availability of the drug is inconsistent between time periods. These results are in accordance with fluctuations in methamphetamine loads from other northern countries in Europe (González-Mariño et al., 2020). Methamphetamine is mainly produced in the Czech Republic which has led to high use of the drug in central Europe (European Monitoring Centre for Drugs and Drug Addiction, 2020; González-Mariño et al., 2020). Traditionally, methamphetamine is not considered a staple of the Icelandic drug market and its use has been reported to be low compared to other European countries (González-Mariño et al., 2020; Löve et al., 2018). Nevertheless, the results point to a rise in methamphetamine use which is in accordance with reports on increased availability of the drug in Europe (European Monitoring Centre for Drugs and Drug Addiction, 2020). WBE can be a valuable tool in the early detection of changes in the local drug market by identifying rapidly emerging drugs such as methamphetamine (Gunnar and Kankaanpää, 2019). Trends between weekends and other weekdays in methamphetamine use varied considerably between sampling weeks ranging from no increase to 93% increase during the weekend. Methamphetamine use by WBE during the music festival held in November 2017 did not show significant trends compared to normal weeks. These results indicate that methamphetamine is not used recreationally during weekends or special events to a large extent.

An increase by 140% was observed in the number of DUI cases positive for methamphetamine from 2014 to 2019 (from 75 to 180 cases) but decreased by 31% from 2019 to 2020 (from 180 to 125 cases) (Fig. 2). As for amphetamine, the total number of performed tests increased by 40% from 2014 to 2020. The decrease detected in 2020 is likely due to a reduction in commuting time during the COVID-19 pandemic. Nevertheless, these results support data by WBE that methamphetamine use is increasing in Iceland, although low compared to amphetamine.

Data on seized amounts of methamphetamine from 2014 to 2019 in powder form is presented in Fig. 3. In 2014 and the years before, seized amounts of methamphetamine powder remained almost non-existent. However, in 2015 seized amounts of methamphetamine began to increase, although still very low compared to amphetamine. Sporadic seizures in recent years, although small, could further indicate that the use of methamphetamine in Iceland is increasing, supporting data by WBE and DUI cases.

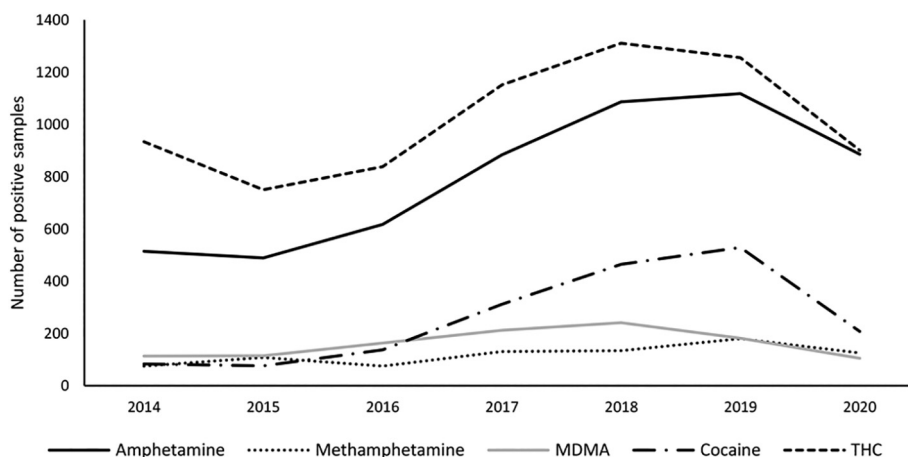


Fig. 2. The number of positive DUI cases for amphetamine, methamphetamine, MDMA, cocaine and cannabis in Iceland from 2014 to 2019.

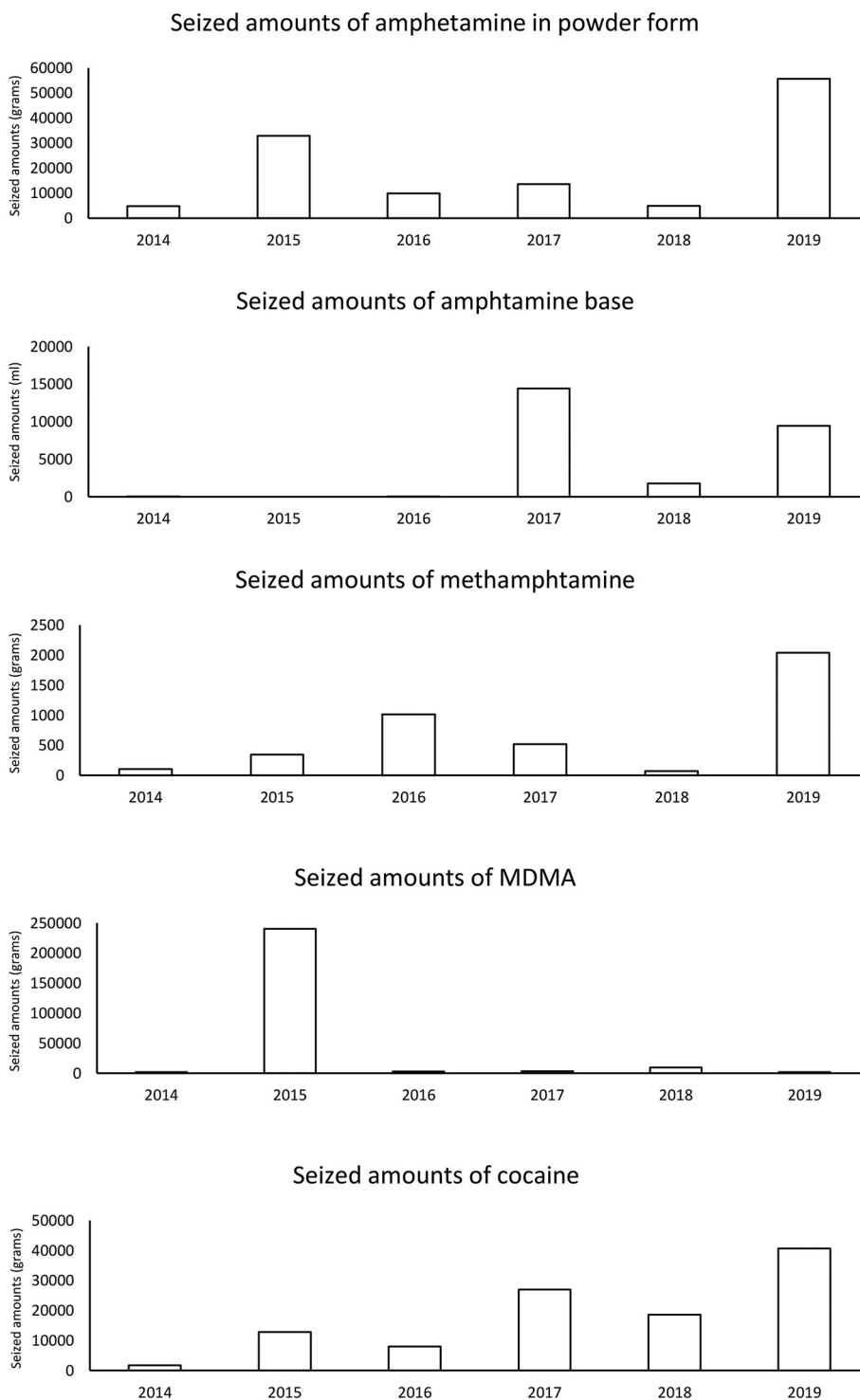


Fig. 3. Seized amounts of amphetamine (powder form and base), methamphetamine (powder form), MDMA (powder form) and cocaine (powder form) by the Icelandic police from 2014 to 2019.

3.4. MDMA

Results from the analysis of MDMA in wastewater samples collected in Reykjavik from February 2017 to June 2020 are presented in Fig. 1. Estimated MDMA use by WBE was close to constant during the total sampling period of this study (from 175 to 194 mg/day/1000 inhabitants). These results are consistent with other European studies based on prevalence data showing stable trends in MDMA use in recent years (European Monitoring Centre for Drugs and Drug Addiction,

2020). Nevertheless, an upsurge in MDMA loads in wastewater from other European countries have been observed which could be explained by increased purity of the drug (González-Mariño et al., 2020). In recent years, MDMA loads from Reykjavik have been in the medium range compared to other European cities (González-Mariño et al., 2020). MDMA use in June 2020 was stable compared to other sampling periods which indicates that the COVID-19 pandemic had not affected the amount of MDMA used in Reykjavik at that time point. The use of the drug seems to have moved to smaller social gatherings in private

homes causing the use to remain unchanged. These results could indicate that MDMA use in Reykjavik during the pandemic can not only be associated with recreational use. Nevertheless, MDMA use increased significantly ($p < 0.05$, t -test) on weekends compared to other weekdays during all sampling periods, ranging from 42% to 154%. This strongly suggests that the drug is largely used recreationally which is in accordance with previously published studies (Löve et al., 2018; Ort et al., 2014; Thomas et al., 2012). An increase in MDMA use was also observed in November 2017 when a music festival was held in Reykjavik. MDMA use during the festival increased by 193% from Saturday to Sunday compared with other weekdays. These trends strongly indicate that MDMA is used as a recreational drug in Iceland during special events as well as weekends. These findings are supported by other European studies on the recreational use of MDMA during special events (Krizman-Matic et al., 2019; Mackulak et al., 2019).

The number of DUI cases with positive MDMA results increased by 61% from 2014 to 2019 (from 113 to 182 cases) but decreased by 42% from 2019 to 2020 (from 182 to 105 cases) (Fig. 2). The total number of performed tests increased by 40% from 2014 to 2020 and therefore the data cannot confirm an increase in MDMA use. A probable cause for the decreased number of positive DUI cases detected in 2020 are the effects of the COVID-19 pandemic. Reduced opening hours of nightclubs and fewer special event may have led the drug use to take place in private homes with less commuting. These results are reasonably consistent with data by WBE which indicate stable MDMA use from the beginning of 2017.

Seized amounts of MDMA remained relatively low throughout the six-year period from 2014 to 2019, presented in Fig. 3. Nevertheless, a significant peak in seized amounts was observed in 2015 but otherwise, negligible amounts of MDMA were seized from 2016 to 2019. Stable use of MDMA since 2017 according to data by WBE suggests that the drug is imported into the country without being discovered by the authorities.

3.5. Cocaine

Cocaine is excreted mostly as the metabolite benzoylecgonine. Consumed amounts of cocaine were calculated based on benzoylecgonine concentrations in wastewater. Results on cocaine use in Reykjavik from February 2017 to June 2020 by WBE are presented in Fig. 1. Cocaine use by WBE increased significantly ($p < 0.05$, t -test) by 139% from February 2017 to April 2019 (from 1110 to 2660 mg/day/1000 inhabitants). The largest increase was by 61% between March 2018 and April 2019 (from 1650 to 2660 mg/day/1000 inhabitants). These results indicate an upward trend in cocaine use in Reykjavik which is in accordance with other European reports on record breaking numbers of seizures (European Monitoring Centre for Drugs and Drug Addiction, 2020; González-Mariño et al., 2020). In recent years, cocaine loads from Reykjavik have been on the rise compared to loads from other European cities and are now in the upper range (González-Mariño et al., 2020). Increasing availability of cocaine in Europe has led to higher purity of seized drugs in Iceland as well as lower prices (European Monitoring Centre for Drugs and Drug Addiction, 2020; National Police Commissioner of Iceland, 2019). However, seized amounts of cocaine in Iceland are based on large seizures by the police and customs but the purity at street level is not analyzed and therefore not known. Consequently, it cannot be confirmed that higher purity of the drug on the street is causing rising levels in wastewater but is likely a contributing factor. Increased availability of cocaine can also be seen in higher numbers of patients in rehabilitation centers in Iceland due to cocaine dependencies (Tyrfingsson, 2019). The improving economic status in Iceland due to expanding tourism could also lead to increased use of cocaine as a similar trend was observed before the financial crash in Iceland in 2008 (Tyrfingsson, 2019). Estimated cocaine use by WBE in June 2020 during the COVID-19 pandemic had dropped significantly by 60% ($p < 0.05$, t -test) compared to April 2019 (from 2660 to 1020 mg/day/1000 inhabitants) which indicates a changed consumption pattern of the drug. All nightclubs in Reykjavik had restricted opening

hours in June 2020 due to COVID-19 resulting in a shortage of the usual social gathering connected with recreational use of drugs. These different circumstances seem to have caused consumers to seek other substances or reduce use altogether. Restrictions on international travel could also affect drug trafficking into the country leading to a lower supply of the drug during that time of the pandemic. During all sampling periods, cocaine use estimated with WBE increased over the weekends (from Saturday to Sunday) compared to other weekdays. This increase ranged from 29% to 68% during weekends apart from only a 10% increase in June 2020 during COVID-19. This increase was significant ($p < 0.05$, t -test) during all sampling periods except in June 2020. The trends between weekdays suggest that the drug is used recreationally during weekends which is consistent with previous reports (Löve et al., 2018; Ort et al., 2014; Thomas et al., 2012). A rise in cocaine use was also observed in November 2017 during the music festival when cocaine use increased by 55% (from Thursday to Sunday) compared to other weekdays. These findings further indicate recreational use of cocaine in Reykjavik during special events supporting other European studies (Krizman-Matic et al., 2019; Mackulak et al., 2019).

A more than six-fold increase was observed in the number of DUI cases positive for cocaine between the year 2014 and 2019 (from 83 to 529 cases) but a decrease was observed from 2019 to 2020 by 61% (from 529 to 208 cases) (Fig. 2). The number of positive samples was relatively stable from 2014 to 2016 (from 83 to 137 cases), but then began to increase to a great extent year by year from 2016 to 2019 (from 137 cases to 529 cases). The decrease detected during the COVID-19 pandemic in June 2020 corresponded with data by WBE. But the total number of performed test more than doubled from 2014 to 2020 which must be taken into account. Nevertheless, this data shows clear signs of increased cocaine use in Iceland corresponding with data by WBE.

Data on seized amounts of cocaine began to rise in 2014, reaching a maximum amount in 2019 with a 23-fold increase from 2014 (from 1.7 kg to 41 kg) as shown in Fig. 3. Along with the extensive rise in the number of positive DUI cases and cocaine amounts in wastewater, these results strongly indicate a large increase in cocaine use in Reykjavik, both in the number of consumers and/or the concentration of the drug. This could be explained by increased availability of the drug and therefore decreased prices (National Center of Addiction Medicine, 2020; National Police Commissioner of Iceland, 2019). Comparison of data by WBE and the purity of cocaine at street level, currently not available, would give more accurate and detailed information where a distinction between trends in the number of users versus the purity of drugs would be possible.

3.6. Cannabis

Cannabis use was calculated based on THCA concentrations in wastewater. Analytical challenges in the determination of THCA in wastewater have been associated with its physio-chemical properties which differ from other illicit drugs and their metabolites (Hernández et al., 2018; Senta et al., 2014). Sources of bias related to the analysis of THCA in wastewater have been identified. Enhanced transformation and sorption to solid particulate matter and biofilm in sewers could cause underestimation of results (McCall et al., 2016). According to these known pre-analytical challenges, several steps were taken to minimize loss of THCA by avoiding filtration and acidification of samples (Causanilles et al., 2017). Wastewater samples were kept frozen at neutral pH until analysis to minimize adsorption. THCA has a very low excretion rate in urine after smoking due to high metabolism of THC. A correction factor of 182 was used in back-calculations based on excretion after smoked administration as it is the most common route for cannabis in Iceland (Gracia-Lor et al., 2016). The extremely low excretion rate of THCA results in uncertainties related to back-calculated consumed amounts which should be interpreted with care. Results on cannabis use in Reykjavik from February 2017 to June 2020 by WBE

are presented in Fig. 1. Cannabis use by WBE remained relatively stable from February 2017 to April 2019 (from 13.7 g/day/1000 inhabitants to 17.8 g/day/1000 inhabitants). These results correspond with reports on cannabis use in Europe amongst young people which have either shown stable or increasing trends in recent years (European Monitoring Centre for Drugs and Drug Addiction, 2020). A 35% increase ($p = 0.0573$, t -test) in cannabis use was observed in June 2020 during the COVID-19 pandemic (from 17.8 g/day/1000 inhabitants to 21.2 g/day/1000 inhabitants). This indicates a change in the consumption pattern of cannabis in Reykjavik during the pandemic with restricted opening hours of nightclubs and possibly increased consumption in private homes. Trends between weekdays did not show any significant changes between weekends and other weekdays from 2017 to 2019. No change in cannabis use was observed during the music festival held in November 2017. These results suggest that the use of products containing THC in Iceland is stable and points to daily use of the drug rather than recreational use. Low amounts due to recreational use could therefore be undetectable due to much larger amounts being used daily. In June 2020 during the pandemic, cannabis use showed a significant increase by 42% ($p < 0.05$, t -test) during the weekend. This further indicates a shift in the consumption patterns of illicit drugs during the COVID-19 pandemic where recreational use of stimulant drugs such as cocaine has been replaced to some extent with cannabis use in private homes. Nevertheless, it should be emphasized that only one 7-day sample collection was performed during the COVID-19 pandemic and therefore does not represent the total period of the pandemic.

Considerable fluctuations were observed in the number of DUI cases positive for THC from 2014 to 2020, shown in Fig. 2. The number of DUI cases decreased from 2014 to 2015 by 20% (from 934 to 750 cases), then increased steadily from 2015 to 2018 by 75% (from 750 to 1310 cases) but was stable from 2018 to 2019 (from 1310 to 1260 cases). In 2020, positive DUI cases decreased again by 28% (from 1260 to 901 cases). A change in commuting patterns during the COVID-19 pandemic is a likely explanation to the decreased number of DUI cases. The total number of performed tests increased by 48% from 2014 to 2019 but had decreased by 30% in 2020. Taking these fluctuations into account, an upwards trend in positive DUI cases was observed from 2015 to 2019. Nevertheless, the overall results support data obtained with WBE which indicate stable cannabis use since the beginning of 2017.

Data on seized amounts of cannabis from 2014 to 2019 is presented in Fig. 4. No significant trends were observed in seized amounts of cannabis plants or marijuana, with substantial fluctuations between 2014 and 2019. Nevertheless, a 17-fold increase in seized amounts of hash was observed during the same six-year period. Although the increase in seized amounts of hash is extensive, they remain low compared with cannabis products obtained from local cultivation. A shift from illegal import of cannabis products into the country to local cultivation was

observed after the financial crash in Iceland in 2008 (National Police Commissioner of Iceland, 2019). This was determined by the low proportion of seized amounts of cannabis at the national border compared to seized amounts of cannabis from local production sites. Following the financial crash, seized amounts of hash began to decrease and have remained low since then. At the same time, an increase was observed in seized amounts of locally produced plants. These trends suggest that marijuana is preferred over hash by Icelandic consumers but the reason for this shift in the Icelandic drug market is unknown. Data on THC content in these different cannabis products was not available for comparison and therefore it was not possible to determine if this was a causing factor. But with large amounts of locally cultivated cannabis the supply and demand is both stable and high in Iceland which corresponds with data by WBE showing stable use since 2017 (National Police Commissioner of Iceland, 2019).

4. Conclusions

A comparison between three indicators of illicit drug use in Iceland has been successfully achieved. Data based on three different indicators of drugs use were compared. Data based on WBE includes all use of illicit drugs, both recreational drug users and users with dependencies. However, data on DUI cases is more likely to only represent problem users. The comparison with seized amounts gives additional information on the availability of drugs on the market but information on the purity of drugs at street level would add more value to these comparisons in future studies. By comparing multiple indicators of drug use, a more comprehensive picture of the drug problem in Iceland can be obtained.

Results show an increase in amphetamine use in recent years according to all indicators, with an increase in local production and a stable supply of the drug. Similar results were shown for methamphetamine, a relatively new drug on the Icelandic drug market, with increasing use according to all indicators, but remains low compared to amphetamine. Minimal trends were observed for MDMA with relatively stable use, but the indication of recreational use was evident. An extensive rise in cocaine use has been observed according to all indicators, likely due to increased availability of the drug and/or decreased prices. A decrease in cocaine use was detected during the COVID-19 pandemic indicating a change in patterns of use. Evidence of recreational use of cocaine was also apparent.

For the first time, WBE has been applied to estimate temporal trends in cannabis use in Iceland which showed comparable trends with the number of DUI cases and seized amounts. Overall, stable trends were observed in cannabis use, but an increase was detected during the COVID-19 pandemic. According to the results a shift in cannabis use was observed after the financial crash in 2008 with a large increase in locally cultivated cannabis but has remained stable in recent years.

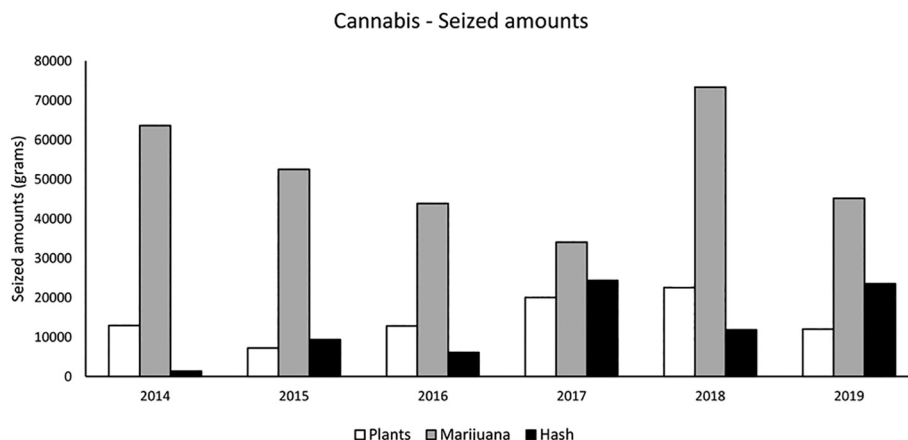


Fig. 4. Seized amounts of cannabis products by the Icelandic police from 2014 to 2019.

These results show that by applying WBE provides crucial additional data on illicit drug use in Iceland in comparison with other indicators such as the number of DUI cases and seized amounts of drugs. All indicators combined painted a similar picture and provided important information on illicit drug use in Iceland.

CRediT authorship contribution statement

Arndís Sue Ching Löve: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Writing – original draft, Visualization. **Valþór Ásgrímsson:** Resources, Methodology, Writing – review & editing, Visualization. **Kristín Ólafsdóttir:** Conceptualization, Methodology, Resources, Writing – review & editing, Visualization, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.scitotenv.2021.149795>.

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